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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,653	11/21/2003	Thomas P. Jerussi	4821-529-999	9144

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EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/717,653	JERUSSI, THOMAS P.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 May 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *41-51*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611

/C.R./ Examiner, Art Unit 1611

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's argument that the cited references fail to teach or suggest the instant claimed enantiomerically pure (S) didesmethylsibutramine is not found to be persuasive because it is the examiner's position that it would have been obvious to a person of skill in the art at the time the invention was made to attempt (or try) to isolate and use the enantiomerically pure (S) didesmethylsibutramine form of the racemate compound as taught by Scott et al. to treat a patient with narcolepsy for its purity. Besides, Young et al. suggest that enantiomerically pure sibutramine and racemate sibutramine, which have the same core structure as the instantly claimed compound, possess the same spectrum of therapeutic activity (page 2, lines 2-4; page 4, lines 1-10; page 10, lines 8-32; and page 17, lines 34-42). Further, Scott et al. suggest that desmethylsibutramine and didesmethylsibutramine have similar pharmacologic activity as the parent compound (= sibutramine; page 97, col. 1, lines 11-20) and Young et al. suggest that optically pure (-) sibutramine is useful for treating disorders ameliorated by inhibition of neuronal monoamine reuptake (e.g. depression) since the pure (-) sibutramine avoids the adverse effects associated with racemic sibutramine (page 17, line 34 to page 18, line 32). Hence, one would have been motivated to attempt to treat a patient with narcolepsy with pure (S) didesmethylsibutramine for its purity because Young et al. suggest that pure (-) sibutramine possess the same therapeutic profile as racemic sibutramine without the adverse effects associated with said racemate and didesmethylsibutramine as taught by Scott et al. is believed to be responsible for the anti-depressive effects of sibutramine (page 97, lines 11-20). Hence, one would reasonably expect to successfully use of the enantiomerically pure(S) didesmethylsibutramine to control the symptoms of depression in a patient with narcoplesy since the pure (S) didesmethylsibutramine and the pure (-) sibutramine have similar structures and compounds with similar structures are expected to have similar pharmacologic utility (MPEP 2144.08-2144.09).

Also, one would reasonably expect to successfully isolate the (S) enantiomer didesmethylsibutramine in view of the teaching of Young et al. (i.e. method of separating isomers of sibutramine; page 17, line 34 to page 18, line 32) and attempt to treat a patient with narcolepsy with said (S)- didesmethylsibutramine isomer to control the symptoms of depression because both Young and Scott et al. suggest that sibutramine compounds are useful to treat depression and Adda et al. suggest that there is a nexus between narcolepsy and depressive symptoms. Hence, contrary to applicant's argument that the options of isolating/selecting of (S)- didesmethylsibutramine isomer and treating a patient with narcolepsy- associated depression with said (S)- didesmethylsibutramine enantiomer do not constitute "a finite number of identified, predictable solutions, with a reasonable expectation of success," it is the examiner's position said options do constitute a finite number of identified, predictable solutions, such that one of skill in the art would have found it obvious to try said options with a reasonable expectation of success. Further, applicant's argument that none of the cited references disclose or suggest the enantiomerically pure (S) didesmethylsibutramine or anything about the use of an anti-depressant for the treatment of narcolepsy is not found to be persuasive for the above the same reasons stated above (MPEP 2141; see also KSR 550 US at ___, 82 US USPQ2d at 1396),.

Further, applicant's argument that steriochemical purity cannot be used as a basis to render the instant claims obvious is also not found to be persuasive because Scott et al. teach that steriochemical purity is of importance in the field of pharmaceuticals (page 3, lines 23-31) and Young et al. teach a method for separating isomers such as sibutramine (page 17, line 34 to page 18, line 32) such that one would reasonably expect to successfully separate the (S) enantiomer of didesmethylsibutramine from its racemate mixture absence evidence to the contrary.

It is noted that Adda et al. disclose that 25% of narcoplesy patients showed depressive complaints based on the BDI test or 41.7% based on the HAM-D test (i.e. 1 of 4 patients with narcolepsy showed depressive complaintsl; abstract). Although Adda et al. found no correlation between narcolepsy and major depression, the study results show that there is a link between narcolepsy and non-major depression. Further, one would reasonably expect to successfully attempt to treat a narcolepsy patient with mild to moderate depressive complaints to prevent the development of major depression and psychosocial impairment rather than wait until the minor/moderate depressive complaints development into major depressive symptoms. Thus, the absent of evidence of a correlation between narcolepsy and major depression as disclosed by Adda et al. does not belie the fact that there is a nexus between narcolepsy and mino/moderate depressvie complaints. Since Scott et al. and Young et al. teach that sibutramine compounds are useful to treat depression, one would have expected to successfully obtain the pure (S)-didesmethylsibutramine from the didesmethylsibutramine racemate taught by Scott et al. via the isomer separation method taught by Young et al. for use to treat a narcolepsy patient with minor/moderate depressive symptoms in narcoplesy patients with depressive complaints. Hence, applicantt's argument that Adda et al. does do eatablish a ling between narcolepsy and depression is not found to be persuasive in view of the teaching of Adda et al. that 25% of narcoplesy patients showed depressive complaints based on the BDI test or 41.7% based on the HAM-D test (i.e. 1 of 4 patients with narcolepsy showed depressive complaintsl; abstract). Since there is a nexus between narcolepsy and depression and Scott et al. suggest that (S) didesmethylsibutramine may have similar properties as the racemate form (such as anti-depressive effects), the treatment of depression in a patient with narcolepsy is a treatment of narcolepsy. Besides, applicant has not specified what symptoms are treated in the scope of the claim.

With respect to applicant's argument that Adda et al. fail to teach or suggest the treatment of narcolepsy (because any administration of an anti-depressant would have been for the purpose of treating depression and not for the purpose of treating narcolepsy), this argument is not found to be persuasive since even though not all patients with narcolepsy have symptoms of depression it is routine in the medical arts to treat patients based on patient factors, including severity of disease or symptoms, such that it would have been within the scope of skill and knowledge of an artisan skilled in the art to combine the cited references to treat a patient suffering from narcolepsy, wherein said patient also had depressive symptoms associated with narcolepsy as taught by Adda et al., with optically pure (S) didesmethylsibutramine to control the symptoms of depression as Adda et al. suggest that patients with narcolepsy are susceptible to develop depressive symptoms as a complication of their narcoleptic condition (abstract). Hence, applicant's assertion that Adda teaches that there is no correlation between depression and narcolepsy is not found to be persuasive because Adda discloses that depressive complaints are observed in patients with narcolepsy (see Adda, abstract). Besides, the instant claimed narcolepsy population does not preclude a narcolepsy patient from also developing depressive symptoms. To the extent that depressive symptoms are experienced by patients with narcolepsy, it would have been obvious to try to treat a patient with narcolepsy with optically pure (S) didesmethylsibutramine to control the symptoms of depression in said patient because Scott et al. teach that stereochemical purity is of importance in the field of pharmaceuticals

(page 3, lines 23-31) and Young et al. teach a method to isolate isomers of the prior art suggest that the pure (S) didesmethylsibutramine might be preferred over the racemate form.

Contrary to applicant's argument, it is the examiner's position that the facts of the instant case are distinguishable from the facts in Rapoport v. Dement since in the instant case the symptom of depression is not severable from narcolepsy but is related to the underlined narcoleptic condition such that one would reasonably expect to successfully control the symptoms associated with narcolepsy (e.g. depression) with optically pure (S) didesmethylsibutramine absent objective evidence to the contrary.

Thus, the rejection is maintained.